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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/618,157	07/10/2003	Laszlo Vigh	D2198-00008	4058

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EXAMINER	
FEDOWITZ, MATTHEW L	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 10/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/618,157	VIGH ET AL.	
	Examiner	Art Unit	
	Matthew L. Fedowitz	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

T.D

DETAILED ACTION

Claims 1-34 are pending in this action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 32-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Van Duzer et al.

Van Duzer et al. teach compounds that overlap with those compounds broadly claimed by the applicant (see claims 1-9 in columns 36-38). Applicant is encouraged to amend the claims to exclude any overlapping compounds and to include a brief and concise explanation of the claim amendments.

Claim Rejections - 35 USC § 112 First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds where A is substituted with groups disclosed under I', I", 1, 3, 8, 9, 10, 11, 13, 14, 15 and 16 on pages 135-138 of the specification, the specification does not reasonably provide enablement wherein A can be all substituted alkyls , aralkyls, aralkyls

substituted in the aryl and/or alkyl moiety, substituted aryls, heteroaryls or substituted heteroaryl groups. In addition, the specification does not reasonably provide enablement wherein R^3 can be all substituted alkyls, substituted aryls, aralkyl and aralkyl substituted in the aryl and/or alkyl moiety. Or even wherein X can be all substituted imino groups and R' can be all substituted alkyls, substituted aryls, aralkyls having substituted aryls or alkyl moieties or substituted acyl groups.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the factual considerations. In re Wands, 8 USPQ2d 1400 (CAFC). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include but are not limited to:

1. The breadth of the claims;
2. The nature of the invention;
3. The state of the prior art;
4. The level of one of ordinary skill;
5. The level of predictability in the art;
6. The amount of direction provided by the inventor;
7. The existence of working examples; and

8. The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Wands Analysis

1. The Breadth of the Claims.

The breadth of the instant claims are seen to encompass methods comprising a means of increasing expression of a molecular chaperon by an eukaryotic cell comprising: treating an eukaryotic cell of a living mammalian organism that is exposed to a physiological stress accompanying allergic diseases, immune diseases, autoimmune diseases, diseases of viral or bacterial origin, tumorous, skin and/or mucous diseases, epithelial disease of renal tubulus, atherosclerosis, coronarial disease, pulmonary hypertonia, cerebrovascular ischemia, stroke, or traumatic head injury with an effective amount of a chemical compound to increase the expression of the molecular chaperon by the cell beyond the amount induced by the physiological stress, wherein the chemical compound is one or more of a hydroxylamine derivative represented by formula (II).

The breadth of the instant claims are also seen to encompass methods comprising a means of increasing activity of a molecular chaperon in an eukaryotic cell that is exposed to a physiological stress comprising: treating the cell that is exposed to a physiological stress accompanying allergic diseases, immune diseases, autoimmune diseases, diseases of viral or bacterial origin, tumorous, skin and/or mucous diseases, epithelial disease of renal tubulus, atherosclerosis, coronarial disease, pulmonary hypertonia, cerebrovascular ischemia, stroke, or traumatic head injury with an effective amount of a chemical compound to increase the activity

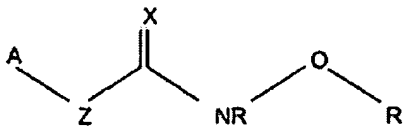
of the molecular chaperon in the cell beyond the amount induced by the physiological stress, wherein the chemical compound is one or more of a hydroxylamine derivative represented by formula (II).

The breadth of the instant claims are further seen to encompass methods comprising a means of treating a disease connected with the function of the chaperon system or associated with the injury of the membrane of a cell or cell organellum or preventing the same which comprises: administering to a host that has been exposed to a physiological stress accompanying allergic diseases, immune diseases, autoimmune diseases, diseases of viral or bacterial origin, tumorous, skin and/or mucous diseases, epithelial disease of renal tubulus, atherosclerosis, coronarial disease, pulmonary hypertonia, cerebrovascular ischemia, stroke, or traumatic head injury an effective amount of a chemical compound to increase the expression of a molecular chaperon by cells of the host beyond an amount induced by the physiological stress to ameliorate the effect caused by the pathological condition in the organism, wherein the chemical compound is one or more of a hydroxylamine derivative represented by formula (II).

In addition, the breadth of the instant claims are seen to encompass hydroxylamine derivative compounds of the formula (II) as well as pharmaceutical compositions thereof.

2. The Nature of the Invention.

The nature of the invention relates to hydroxylamine derivative compounds, compositions and methods of using such compounds. The hydroxylamine derivative compounds have basic formula represented by formula II below.



Formula II

3. The State of the Prior Art.

The applicant discloses several examples of hydroxylamine derivative compounds and the use of some of these compounds. However, the showing of the activity of these compounds does not provide an adequate representation to enable one to claim methods comprising a means of increasing expression of a molecular chaperon by an eukaryotic cell, methods comprising a means of increasing activity of a molecular chaperon in an eukaryotic cell that is exposed to a physiological stress, methods comprising a means of treating a disease connected with the function of the chaperon system or associated with the injury of the membrane of a cell or cell organellum or preventing the same or even the synthesis of all compounds as claimed by the applicant.

As a result of this finding and the lack of adequate guidance or representations in the specification, the applicant has not enabled these aspects of the claimed compounds. The skilled artisan in this field would not accept the representations set forth in the instant disclosure as sufficient to enable methods for using or making hydroxylamine derivative broadly.

4. The Level of Ordinary Skill

The level of skill is that of one with a doctoral understanding of chemical synthesis and therapeutics.

5. The Level of Predictability in the Art

The synthesis of hydroxylamine derivative compounds is unpredictable and is limited by the fact that the claimed substituted groups encompass a vast multitude of compounds. Furthermore, the applicant has claimed that this vast multitude of compounds will be useful for treating numerous disease states. The treatment of these disease states cannot be prospectively treated through the use of such claimed compounds when no examples of such compounds have been used in such a manner. As such, the treatment of these disease states is unpredictable.

6. The Amount of Direction Provided by the Inventor

The applicant has not demonstrated sufficient guidance provided in the form of adequate supporting representations or art recognized correlations in patent or non-patent literature. For example, the applicant only discloses examples on pages 85-134 demonstrating the activity of some of the compounds claimed. However, the applicant has not provided direction in the form of representative examples to show that the combinations of the functional groups claimed would have efficacy in the manner as claimed by the applicant.

7. The Existence of Working Examples

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught

one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 27 USPQ2d 1510 (CAFC). The disclosure does not demonstrate sufficient evidence to support the applicant's claim to use all of the claimed compounds in the methods or to synthesize such compounds. Applicant's broad claims necessarily require a broad disclosure or guidance in the art to accept the methods for the diverse group hydroxylamine derivative compounds claimed.

8. The Quantity of Experimentation Needed to Make or Use the Invention Based on the Content of the Disclosure

In order for compounds and methods comprising hydroxylamine derivatives as defined in formula II, it would be necessary to demonstrate how to make the claimed compounds by providing references that contain directions or examples from which would direct one how to make the claimed compounds as well as how all of the compounds claimed could be used in the methods as claimed by the applicant. The specification submitted and examples therein do not demonstrate this. Therefore, one of ordinary skill in the art would require a significant amount of experimentation in order to make and practice the substituted porphyrin compounds claimed by the applicant.

Claim Rejections - 35 USC § 112 Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, 11, 17, 23, 25, 27, 28, 29, 31, 32, and 34 claim a group defined as R', however, R' does not appear in formula II. There is some indication that R' may be attached to the nitrogen in the structure but due to the poor quality of the printed claims it cannot be determined with certainty that the applicant intends R' to be attached to the nitrogen of formula II. For purposes of examination, the R' group was examined as if it were attached to the nitrogen in formula II.

The applicant is encouraged to submitted amended claims with R' distinctly claimed to facilitate examination.

Claims 2-10, 12-16, 18-22, 24, 26, 30 and 33 are also rejected as they depend from a rejected base claim.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Matthew L. Fedowitz whose telephone number is (571) 272-3105. If attempts to reach the examiner by telephone are unsuccessful, the examiner's primary, James O. Wilson, can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Matthew L. Fedowitz, Pharm.D., Esq.

James O. Wilson, Supervisory Patent Examiner
Art Unit 1623